REMARKS

Claims 1, 7-17, 22, 23, and 27 are pending in the application. Claims 3 and 4 have been cancelled without prejudice by the present response. Claims 1 and 13 have been amended. Support for the amendments can be found in the specification at, e.g., page 5, lines 15-28. These amendments add no new matter.

Rejoinder

At page 2 of the Office Action, the Examiner stated that claims 23 and 27 have been withdrawn from consideration as being drawn to non-elected subject matter. Method claims 23 and 27 depend from and include all of the limitations of composition claim 1. In accordance MPEP § 821.04, applicants request that the Examiner rejoin and examine method claims 23 and 27 upon the allowance of composition claim 1.

Priority

At pages 2-3 of the Office Action, the Examiner stated that claim 16 is entitled to a priority date of April 16, 2004 (the filing date of the present application). In view of the remarks presented herein, applicants respectfully submit that examination of the present application does not require a determination of whether claim 16 is also entitled to the priority dates of application serial number 60/463,284, filed April 16, 2003, and application serial number 60/472,317, filed May 20, 2003.

Claim Objections

At pages 3-4 of the Office Action, claims 1, 3, 4, and 13 were objected to on several bases.

Claims 3 and 4 have been cancelled without prejudice, thereby rendering their objection moot. It is applicants' understanding that the amendments to claims 1 and 13 obviate the remaining objections.

35 U.S.C. § 112, First Paragraph (Enablement)

At pages 4-7 of the Office Action, claims 1, 3, 4, 7-17, and 22 were rejected as not enabled. According to the Office Action

> the specification, while being enabling for a yeast cell comprising two integrated copies of an expression construct comprising a nucleic acid encoding a protein comprising wild-type alpha synuclein or mutant human A53T under control of an inducible promoter wherein the protein is toxic to the cell such that the cell is non-viable, does not reasonably provide enablement for any other embodiment.

Claims 3 and 4 have been cancelled without prejudice, thereby rendering their rejection moot.

Independent claim 1 and the claims that depend therefrom require that expression of the nucleic acid in the yeast cell be regulated by an inducible promoter. Because these claims require the presence of an "inducible promoter," the Examiner's remarks under the present heading do not appear to apply to these claims.

Independent claim 17 is directed to a yeast cell comprising two integrated copies of an expression construct comprising a nucleic acid encoding a protein comprising wild-type human alpha-synuclein or mutant human alpha-synuclein A53T, wherein the cell expresses a toxicity-inducing amount of the protein. The Office Action asserted that "it is not clear how a toxicity inducing amount is achieved in the absence of an inducible promoter given the lethal affect of the protein on the cell." Similarly, the Office Action stated that "[c]onstitutive expression would not allow the cell to mature and grow." The present application describes screening assays for identifying compounds that prevent or suppress toxicity resulting from alpha-synuclein expression in a yeast cell. With respect to those embodiments of claim 17 that encompass constitutive expression of alpha-synuclein, a yeast cell can optionally have a constitutive expression vector introduced into the cell and also be contacted with a candidate compound within a limited time frame so that a compound that prevents or suppresses toxicity has its effect (i.e., rescues the cell) before the otherwise toxic effect of the alpha-synuclein expression takes hold on the cell. As a result, an inducible promoter is not required to practice all embodiments of the claimed invention.

In view of the foregoing remarks, applicants respectfully request that the Examiner withdraw the rejection of independent claims 1 and 17 and the claims that depend therefrom.

35 U.S.C. § 102(e) (Anticipation)

At pages 7-8 of the Office Action, claims 1, 3, 4, 7-15, 17, and 22 were rejected as anticipated by Lindquist et al., U.S. Patent No. 7,045,290 ("Lindquist") as evidenced by Sherman (Nine Yeast Vectors downloaded 7/18/08).

Claims 3 and 4 have been cancelled without prejudice, thereby rendering their rejection moot.

Independent claims 1 and 17 are directed to yeast cells that, among other features recited in the claims, comprise two integrated copies of an expression construct comprising a nucleic acid encoding a protein comprising wild-type human alpha-synuclein or mutant human alpha-synuclein A53T. As detailed in the present application, the inventors have discovered that alpha-synuclein-induced toxicity in yeast is dosage dependent. Yeast cells that contain one integrated copy of an alpha-synuclein gene under the regulation of a galactose-inducible promoter showed moderate growth defects whereas cells with two copies exhibited extreme defects (see specification at page 2, lines 16-25 and page 40, line 20, to page 41, line 3).

Lindquist discloses that expression of wild-type human alpha-synuclein or mutant human alpha-synuclein A53T in yeast is toxic to the cells. However, Lindquist does not describe yeast cells containing two integrated copies of a construct encoding alpha-synuclein, as is required by the claims of the present application. The Office Action cited column 21 of Lindquist as describing vectors that "allow integration of two copies or more as recited in claims 2 and 19." For sake of clarification, the present application does not contain pending claims numbered 2 and 19. Furthermore, column 21 of Lindquist does not describe construction of the cells used by Lindquist in the experiments depicted in Figure 3. The section in column 21 entitled "Integrating plasmids" describes an exemplary plasmid (Y1p) that is maintained at one copy per haploid genome (see column 21, lines 11-13). Column 21 of Lindquist contains extensive description of many types of nucleic acid vectors (many of which are autonomously replicating vectors – i.e.,

not integrating vectors) that can be used for expression of proteins identified by the generic term "misfolded disease protein." There is no description in column 21 of preparation of a yeast cell that contains two integrated copies of an expression construct encoding alpha-synuclein. As a result, Lindquist does not anticipate independent claims 1 or 17 or the claims that depend therefrom. Applicants respectfully request that the Examiner withdraw the rejection.

35 U.S.C. § 103(a) (Obviousness)

At pages 8-10 of the Office Action, claim 16 was rejected as unpatentable over Lindquist in view of Frate, U.S. Published Application No. 20040115792.

Claim 16 depends from claim 14 (which depends from independent claim 1) and requires that the claimed yeast cell contain a disruption in the PDR5 gene.

The Office Action cited Frate as describing "use of a yeast cell line comprising a disruption of PDR5 for testing genotoxicity and cytotoxicity of environmental contaminants." As detailed above in response to the anticipation rejection, Lindquist does not disclose the yeast cell of independent claim 1. Frate provides nothing that supplements the deficiencies of Lindquist or renders obvious independent claim 1. Accordingly, once independent claim 1 is held allowable, dependent claim 16 should also be in condition for allowance.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are in condition for allowance, which action is requested.

Enclosed is a Petition for Three Month Extension of Time. The extension of time fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply other any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 17481-003001.

Respectfully submitted,

Date: January 26, 2009

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